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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/014,519  | 12/14/2001  | Betty Wu             | 19662-029001        | 3927             |
| 26161   | 7590        | 09/22/2006           | EXAMINER            |                  |
| FISH & RICHARDSON PC<br>P.O. BOX 1022<br>MINNEAPOLIS, MN 55440-1022 |             |                      | SINES, BRIAN J      |                  |
|   |             | ART UNIT             | PAPER NUMBER        |                  |
|   |             | 1743                 |                     |                  |

DATE MAILED: 09/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                                   |                         |  |
|------------------------------|-----------------------------------|-------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b>            | <b>Applicant(s)</b>     |  |
|                              | 10/014,519                        | WU ET AL.               |  |
|                              | <b>Examiner</b><br>Brian J. Sines | <b>Art Unit</b><br>1743 |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 6/26/2006.
- 2a) This action is **FINAL**.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-4,9,12-14,16,18,19,21-23,25-30,32,33,35-37 and 39-51 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) 16,18,19,22,-23,25,26,33,35-37,41-44,48 is/are allowed.
- 6) Claim(s) 1-4,9,27-30,32,39,40,45-47 and 49-51 is/are rejected.
- 7) Claim(s) 12-14 and 21 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) Notice of Informal Patent Application
- 6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Claim Objections***

Claims 21 and 46 are objected to because of the following informalities: Claim 21 is dependent on canceled claim 17 (claim 21 is assumed to be dependent on claim 16 for examination purposes). Claim 46 is dependent on itself (claim 46 is assumed to be dependent on claim 45 for examination purposes). Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

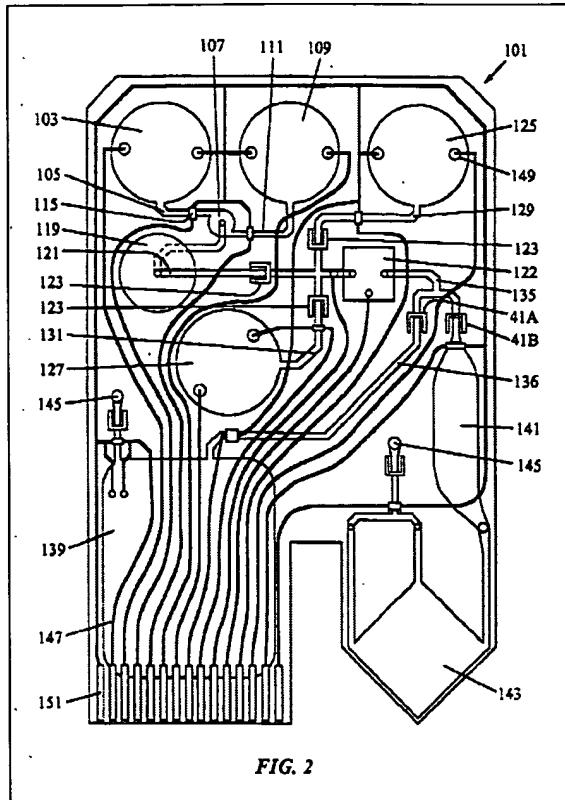
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 – 4, 9, 27 – 30, 32, 39, 40, 45 – 47 and 49 – 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pourahmadi et al. (U.S. Pat. Pub. No. US 2002/0055167 A1) (hereinafter “Pourahmadi”) in view of Handique et al. (U.S. Pat. No. 6,130,098 A) (hereinafter “Handique”).

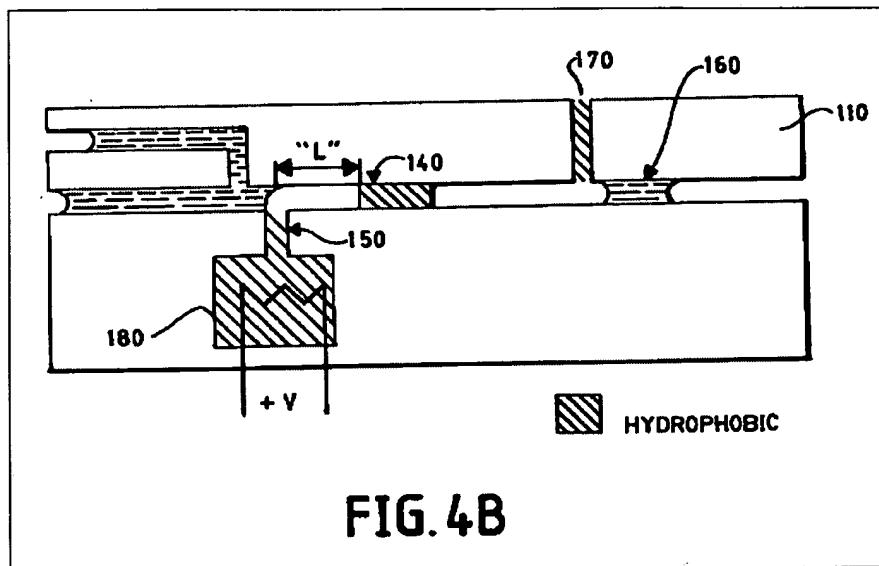
Regarding claims 1, 9, 39 and 47, Pourahmadi teaches an apparatus (cartridge 101) comprising: a sample port (103); a channel (105); and a lysing zone (lysing chamber 119) (see paragraph 0048; figure 2).



Pourahmadi does not specifically teach the further incorporation of a gas actuator and an associated vent structure to facilitate sample fluid flow within the disclosed apparatus. Pourahmadi does teach that a fluid sample may be introduced into the cartridge by a variety of means, manual or automated (see paragraph 0078). Pourahmadi teaches that for automated sample introduction, additional cartridge design features are employed and, in many cases, impart specimen accession functionality directly into the cartridge (see paragraph 0080). Pourahmadi does further teach that a fluid motive source comprising a pneumatic pressure

source can be internally incorporated within the cartridge apparatus for facilitating sample fluid transport (see paragraph 0067).

Handique teaches a thermopneumatic apparatus for facilitating fluid transport in microfluidic devices (see col. 13, line 60 – col. 15, line 40; figures 3A, 3B, 4A & 4B). As shown in figure 4B, the system taught by Handique comprises a thermopneumatic actuating system denoted by 180, a hydrophobic gas vent (170), and an outlet, which is located to the right of the sample (160) and at the end of the channel containing the sample, from which the sample is transferred for further processing, such as to a lysing chamber for cell lysing, when integrated within an analytical microfluidic system.



Hence, as evidenced by Handique, a person of ordinary skill in the art would accordingly have had a reasonable expectation for success in incorporating such a thermopneumatic fluid transport system with a microfluidic apparatus. The Courts have held that the prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. See *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.

1986) (see MPEP § 2143.02). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate such a thermopneumatic fluid transport system with a microfluidic apparatus for facilitating effective sample fluid transport.

Furthermore, regarding claim 39, Pourahmadi in view of Handique teaches the additional incorporation of a positioning element (e.g., a hydrophobic region 140) and a thermopneumatic actuator downstream of the lysing chamber 119 for facilitating sample fluid flow within the apparatus for further processing (see figure 2). Pourahmadi teaches that the lysed sample proceeds from the lysing chamber 119 down channel 121 and is forced to flow through a capture component 122 (see paragraph 0070; figure 2). Hence, a person of ordinary skill in the art would have recognized the suitability of incorporating a fluid motive source, such as the thermopneumatic system of Handique, within the apparatus of Pourahmadi to facilitate effective sample fluid transport (see MPEP § 2144.07). As discussed above, as evidenced by Handique, a person of ordinary skill in the art would accordingly have had a reasonable expectation for success in incorporating such a thermopneumatic fluid transport system with a microfluidic apparatus (see MPEP § 2143.02). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate a secondary thermopneumatic fluid transport system with a microfluidic apparatus as claimed for facilitating effective sample fluid transport.

Regarding claim 2, these claim recitations are considered statements of intended use.

Regarding claims 3, 4, 45 and 46, Pourahmadi teaches the incorporation of a cell lysis mechanism utilizing an electrical field to facilitate cell lysis and extraction (see paragraph 0112). Furthermore, the use of pulse circuits with cell lysis mechanisms using electrical fields are well known in the art.

Regarding claims 39 and 49 – 51, Handique suggests the incorporation of valves, which are well known in the art, with the hydrophobic vents (70 & 170) for opening and closing the vents for facilitating sample fluid transport (see col. 14, lines 51 – 57; figures 3A, 3B, 4A & 4B) (see MPEP 2144.03). Handique also teaches the use of thermally-actuated valves (see col. 14, lines 51 – 57; col. 16, lines 40 – 61; figures 3A, 3B, 4A & 4B). In addition, Pourahmadi teaches the incorporation of various valves within the disclosed microfluidic apparatus (see, e.g., paragraph 0052). Therefore, it would have been obvious to a person of ordinary skill in the art to provide a plurality of valves within the apparatus as claimed in order to facilitate effective sample fluid flow within apparatus.

Regarding method claims 27 – 30, 32 and 40, as discussed above, Pourahmadi in view of Handique teaches all of the positively recited structure of the apparatus provided in the claimed method, which merely recites the conventional operation of the features of that apparatus. Therefore, it would have been obvious to a person of ordinary skill in the art to perform the method recited in the instant claims upon the apparatus of Pourahmadi and Handique,

***Allowable Subject Matter***

Claims 16, 18, 19, 22, 23, 25, 26, 33, 35 – 37, 41 – 44 and 48 are allowed.

The following is an examiner's statement of reasons for allowance:

Regarding claim 16, the cited prior art neither teach nor fairly suggest a microfluidic device incorporating the gas actuator and positioning element configuration as claimed.

Regarding claim 33, the cited prior art neither teach nor fairly suggest a method for lysing and separating a microdroplet of cell-containing liquid using a microfluidic device as claimed.

Claims 12 – 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled “Comments on Statement of Reasons for Allowance.”

***Response to Arguments***

Regarding the rejection of the present claims under 35 U.S.C. 103(a) as being unpatentable over Pourahmadi in view of Handique, applicant's arguments filed 6/26/2006 have been fully considered but they are not persuasive. The applicant alleges that the combined references do not teach each and every limitation of the claimed invention. The applicant alleges that the two devices taught by the prior art operate using different fluid transport mechanisms. In response to applicant's argument that the disclosed teachings of each of the references are essentially incompatible since Pourahmadi teaches a continuous flow-type device and Handique teaches a device that operates by manipulating microdroplets, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based

on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, both references pertain to microfluidic device that process similar samples for analysis. The prior art devices differ essentially in the fluid transport mechanisms used within each device. Pourahmadi does teach that the disclosed apparatus is capable of processing sample volumes of 10  $\mu$ L or less (see paragraphs 0077 and 0163). Pourahmadi does teach that current microfluidic devices are capable of processing large, i.e., microliter, and small sample volumes, i.e., picoliter and nanoliter fluid volumes (see paragraphs 0007 – 0010; figure 1). Pourahmadi does indicate that the disclosed device is capable of performing immunoassays that, as shown in figure 1, use approximately nanoliter sample volumes and less (see paragraph 0087). Handique also teaches the use of sample volumes of between approximately 0.01 and 100 nanoliters (see col. 7, lines 53 – 63). Thus, both microfluidic devices can process similar sample volumes. Furthermore, both disclosed microfluidic devices can be made using the same fabrication techniques, e.g., photolithography (see Handique, col. 4, lines 7 – 10; Pourahmadi, paragraph 0098). Pourahmadi does teach the use of fluid flow mechanisms, such a pump, integrated within the device itself (see paragraphs 0020 and 0139). Thus, a person of ordinary skill in the art would accordingly

have had a reasonable expectation for success in incorporating such a thermopneumatic fluid transport system, as taught by Handique, with the microfluidic apparatus of Pourahmadi. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage, or expected beneficial result would have been produced by their combination. See *In re Sernaker*, 702 F.2d 989, 994 – 995, 217 USPQ 1, 5, 6 (Fed. Cir. 1983) (see MPEP § 2144). The Court has recognized that an artisan is presumed to have skill, rather than lack of skill. See *In re Sovish*, 226 USPQ 771 (Fed. Cir. 1985). In addition, the rationale to support an obviousness rejection under 35 U.S.C. 103 may rely on logic and sound scientific principle (see MPEP § 2144.02). Handique does teach that the disclosed fluid transport mechanism significantly improves fluid sample processing overcoming liquid handling inefficiencies within conventional analytical microfluidic devices (see col. 3, lines 33 – 64). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate such a thermopneumatic fluid transport system with the disclosed microfluidic apparatus as claimed for facilitating effective sample fluid transport and processing.

Regarding the rejection of claims 12 – 14, 16, 18, 19, 22, 23, 25, 26, 33, 35 – 37, 41 – 44, Applicant’s arguments filed 6/26/2006 have been fully considered and are persuasive. This rejection has been withdrawn.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Sines, whose telephone number is (571) 272-1263. The examiner can normally be reached on Monday - Friday (11 AM - 8 PM EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read "Brian J. Kim". The signature is fluid and cursive, with "Brian" on the left and "J. Kim" on the right, separated by a diagonal line.